



Docket No.: 17243/004001

(PATENT)

#### IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Letters Patent of: Heinz W. Gschwend et al.

Patent No.: 7,514,436

Issued: April 7, 2009

For: PYRIDAZINE DERIVATIVES AND THEIR

**USE AS THERAPEUTIC AGENTS** 

# REQUEST FOR CERTIFICATE OF CORRECTION PURSUANT TO 37 CFR 1.322

Attention: Certificate of Correction Branch Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450

Dear Sir:

Upon reviewing the above-identified patent, Patentee noted typographical errors which should be corrected.

In the Claims:

MAY 1 4 2009

In Claim 1, column 40, line 22, " $R_{7a}$ " should be  $-R^{7a}$ —.

In Claim 15, column 43, line 17, " $C_7$ - $C_{12}$ " should be -- $C_2$ - $C_{12}$ --.

In Claim 21, column 44, line 14, "{-[6-(Methyl-phenethyl-amino)pyridazin-3-yl]" should be --{4-[6-(Methyl-phenethyl-amino)-pyridazin-3-yl]--.

In Claim 27, column 45, line 13, the word "hydroxyl" should be -hydroxy-.

In Claim 27, column 45, line 17, the word "hydroxyl" should be -hydroxy-.

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In Claim 27, column 45, line 17, "C1-C6trihaloalkyl and" should be

--C<sub>1</sub>-C<sub>6</sub>trihaloalkyl,-.

In Claim 28, column 46, line 9, the word "amoun" should be -amount-.

The errors were not in the application as filed by applicant; accordingly no fee is

required.

Transmitted herewith is a proposed Certificate of Correction effecting such

amendment. Also enclosed, as evidence of the errors, is a copy of the claims as issued, and a

copy of the Claims as allowed. Patentee respectfully solicits the granting of the requested

Certificate of Correction.

Applicant believes no fee is due with this request. However, if a fee is due,

please charge our Deposit Account No. 50-0591, under Order No. 17243/004001.

Dated: May 8, 2009

Respectfully submitted,

T. Chyau Liang, Ph.D.

Registration No.: 48,885

OSHA · LIANG LLP

909 Fannin Street, Suite 3500

Houston, Texas 77010

(713) 228-8600

(713) 228-8778 (Fax)

Fatty acids are analyzed as follows: The reaction mixture is saponified with 10% KOH to obtain free fatty acids which are further methylated using BF3 in methanol. The fatty acid methyl esters are analyzed by high performance liquid chromatography (HPLC) using a Hewlett Packard 1090, Series II 5 chromatograph equipped with a diode array detector set at 205 nm, a radioisotope detector (Model 171, Beckman, CA) with a solid scintillation cartridge (97% efficiency for 14Cdetection) and a reverse-phase ODS (C-18) Beckman column (250 mmx4.6 mm i.d.; 5 μm particle size) attached to a 10 pre-column with a µBondapak C-18 (Beckman) insert. Fatty acid methyl esters are separated isocratically with acetonitrile/water (95:5 v:v) at a flow rate of 1 mL/min and are identified by comparison with authentic standards. Alternatively, fatty acid methyl esters may be analyzed by capillary 15 column gas-chromatography (GC) or Thin Layer Chromatography (TLC).

Those skilled in the art are aware of a variety of modifications to this assay that can be useful for measuring inhibition of stearoyl-CoA desaturase activity in microsomes by test 20 compounds.

Representative compounds of the invention showed activity as inhibitors of SCD when tested in this assay. The activity was defined in terms of % SCD enzyme activity remaining at the desired concentration of the test compound.

All of the U.S. patents, U.S. patent application publications, U.S. patent applications, foreign patents, foreign patent applications and non-patent publications referred to in this specification and/or listed in the Application Data Sheet are incorporated herein by reference, in their entirety.

From the foregoing it will be appreciated that, although specific embodiments of the invention have been described herein for purposes of illustration, various modifications may be made without deviating from the spirit and scope of the invention. Accordingly, the invention is not limited except as 35 by the appended claims.

What is claimed is:

#### 1. A compound of formula (I):

$$R^{2}-W \xrightarrow{R^{4}} N^{5} \xrightarrow{R^{5a}} R^{6a} \xrightarrow{R^{6}} R^{7} R^{7a}$$

$$N-V-R^{3}$$

$$R^{2}-W \xrightarrow{R^{9a}} R^{9a} R^{9a} R^{8a}$$

$$R^{2}-W \xrightarrow{R^{9a}} R^{9a} R^{9a} R^{8a}$$

$$R^{2}-W \xrightarrow{R^{9a}} R^{9a} R^{9a} R^{9a}$$

wherein:

x and y are each independently 1;

W is -O, -C(O)O,  $-N(R^1)$ , -S(O), (where t is 0, 1 or 2),  $-N(R^1)S(O)_2$ , -OC(O), or -C(O); V is -C(O), -C(S),  $-C(O)N(R^1)$ , -C(O)O, 55  $-S(O)_2$ , or  $-S(O)_2N(R^1)$ .

each R<sup>1</sup> is independently selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>12</sub>alkyl, C<sub>2</sub>-C<sub>12</sub>hydroxyalkyl, C<sub>4</sub>-C<sub>12</sub>cycloalkylalkyl and C<sub>7</sub>-C<sub>19</sub>aralkyl;

 $R^2$  is selected from the group consisting of  $C_1\text{-}C_{12}$  alkyl, 60  $C_2\text{-}C_{12}$  alkenyl,  $C_2\text{-}C_{12}$  hydroxyalkyl,  $C_2\text{-}C_{12}$  hydroxyalkyl,  $C_2\text{-}C_{12}$  hydroxyalkyl,  $C_3\text{-}C_{12}$  cycloalkyl,  $C_4\text{-}C_{12}$  cycloalkylalkyl, aryl,  $C_7\text{-}C_{19}$  aralkyl,  $C_7\text{-}C_{12}$  heterocyclylalkyl,  $C_3\text{-}C_{12}$  heterocyclylalkyl,  $C_3\text{-}C_{12}$  heteroaryl, and 65  $C_3\text{-}C_{12}$  heteroarylalkyl, provided that when W is —O—,  $R^2$  is not  $C_1\text{-}C_{12}$  alkyl;

or R<sup>2</sup> is a multi-ring structure having 2 to 4 rings wherein the rings are independently selected from the group consisting of cycloalkyl, heterocyclyl, aryl and heteroaryl and where some or all of the rings may be fused to each other;

 $R^3$  is selected from the group consisting of  $C_1\text{-}C_{12}$  alkyl,  $C_2\text{-}C_{12}$  alkenyl,  $C_2\text{-}C_{12}$  hydroxyalkyl,  $C_3\text{-}C_{12}$  cycloalkyl,  $C_3\text{-}C_{12}$  cycloalkyl,  $C_3\text{-}C_{12}$  cycloalkyl,  $C_3\text{-}C_{12}$  cycloalkyl,  $C_3\text{-}C_{12}$  heterocyclyl,  $C_3\text{-}C_{12}$  heterocyclylalkyl,  $C_1\text{-}C_{12}$  heteroaryl and  $C_3\text{-}C_{12}$  heteroarylalkyl, provided that when V is  $-C(O) - \text{ or } -C(O)O - \text{, } R^3 \text{ is not } C_1\text{-}C_{12}$  alkyl;

or R<sup>3</sup> is a multi-ring structure having 2 to 4 rings wherein the rings are independently selected from the group consisting of cycloalkyl, heterocyclyl, aryl and heteroaryl and where some or all of the rings may be fused to each other:

R<sup>4</sup> and R<sup>5</sup> are each independently selected from hydrogen, fluoro, chloro, methyl, methoxy, trifluoromethyl, cyano, nitro or —N(R<sup>13</sup>)<sub>2</sub>;

nitro or —N(R<sup>13</sup>)<sub>2</sub>; R<sup>6</sup>, R<sup>6a</sup>, R<sup>7</sup>, R<sub>7a</sub>, R<sup>8</sup>, R<sup>8a</sup>, R<sup>9</sup> and R<sup>9a</sup> are each independently selected from hydrogen or C<sub>1</sub>-C<sub>3</sub>alkyl; and each R<sup>13</sup> is independently selected from hydrogen or

C<sub>1</sub>-C<sub>6</sub>alkyl; a stereoisomer, enantiomer or tautomer thereof, a pharmaceutically acceptable salt thereof, a pharmaceutical

composition thereof or a prodrug thereof.

2. A compound of formula (Ia):

$$R^{2}-W \xrightarrow{R^{4}} N \xrightarrow{R^{5}} R^{5} \xrightarrow{R^{6}} R^{7} \xrightarrow{R^{7}a} N \xrightarrow{N} V \xrightarrow{R^{9}a} R^{9} \xrightarrow{R^{9}a} R^{9} \xrightarrow{R^{9}a} R^{9}$$
(Ia)

wherein:

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x and y are each independently 1;

W is -O—, -C(O)O—,  $-N(R^1)$ —, -S(O),— (where t is 0, 1 or 2),  $-N(R^1)S(O)$ 2—, -OC(O)— or -C(O)—; V is -C(O)—, -C(S)—,  $-C(O)N(R^1)$ —, -C(O)O—, -S(O)2—, or -S(O)2 $N(R^1)$ —;

each R<sup>1</sup> is independently selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>12</sub>alkyl, C<sub>2</sub>-C<sub>12</sub>hydroxyalkyl, C<sub>4</sub>-C<sub>12</sub>cycloalkylalkyl and C<sub>7</sub>-C<sub>19</sub>aralkyl;

R<sup>2</sup> is selected from the group consisting of C<sub>1</sub>-C<sub>12</sub>alkyl, C<sub>2</sub>-C<sub>12</sub>alkenyl, C2-C12hydroxyalkyl, C2-C12hydroxyalkenyl, C2-C12alkoxyalkyl, C<sub>3</sub>-C<sub>12</sub>cycloalkyl, C<sub>4</sub>-C<sub>12</sub>cycloalkylalkyl,  $C_7$ - $C_{19}$ aralkyl, C<sub>3</sub>-C<sub>12</sub>heterocyclyl, C<sub>1</sub>-C<sub>12</sub>heteroaryl, C<sub>3</sub>-C<sub>12</sub>heterocyclylalkyl, and C<sub>3</sub>-C<sub>12</sub>heteroarylalkyl, provided that, when W is —C(O)—,  $R^2$  can not be  $C_1$ - $C_6$ alkyl substituted by —S(O), $R^{14}$  where  $R^{14}$  is hydrogen,  $C_1$ - $C_6$ alkyl, C7-C12aralkyl, pyrazinyl, pyridinonyl, pyrrolidionyl or imidazolyl, provided that when W is -O-, R2 is not  $C_1$ - $C_{12}$ alkyl;

or R<sup>2</sup> is a multi-ring structure having 2 to 4 rings wherein the rings are independently selected from the group consisting of cycloalkyl, heterocyclyl, aryl and heteroaryl and where some or all of the rings may be fused to each other;



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R^3 is selected from the group consisting of C_1-C_{12}alkyl,
      C<sub>2</sub>-C<sub>12</sub>alkenyl,
                                                   C<sub>2</sub>-C<sub>12</sub>hydroxyalkyl,
C<sub>2</sub>-C<sub>12</sub>alkoxyalkyl,
      C2-C12hydroxyalkenyl,
      C<sub>3</sub>-C<sub>12</sub>cycloalkyl,
                                     C<sub>4</sub>-C<sub>12</sub>cycloalkylalkyl,
                                                     C<sub>3</sub>-C<sub>12</sub>heterocyclyl, 5
      C_7-C_{19}aralkyl,
      C<sub>3</sub>-C<sub>12</sub>heterocyclylalkyl,
                                             C<sub>1</sub>-C<sub>12</sub>heteroaryl
                                                                           and
      C<sub>3</sub>-C<sub>12</sub>heteroarylalkyl, provided that when V is
         -C(O)— or -C(O)O—, R^3 is not C_1-C_{12}alkyl;
  or R<sup>3</sup> is a multi-ring structure having 2 to 4 rings wherein
      the rings are independently selected from the group con- 10
      sisting of cycloalkyl, heterocyclyl, aryl and heteroaryl
      and where some or all of the rings may be fused to each
  R4 and R5 are each independently selected from hydrogen,
      fluoro, chloro, methyl, methoxy, trifluoromethyl, cyano, 15
  nitro or —N(R<sup>13</sup>)<sub>2</sub>;

R<sup>6</sup>, R<sup>6</sup>, R<sup>7</sup>, R<sup>7</sup>, R<sup>8</sup>, R<sup>8</sup>, R<sup>8</sup>, R<sup>9</sup> and R<sup>9</sup> are each independently selected from hydrogen or C_1-C_3alkyl; and
   each R<sup>13</sup> is independently selected from hydrogen or
      C_1-C_6alkyl;
  a stereoisomer, enantiomer or tautomer thereof, a pharma-
      ceutically acceptable salt thereof, a pharmaceutical
      composition thereof or a prodrug thereof.
  3. The compound of claim 2 wherein:
  x and y are each 1;
  W is —O—;
V is —C(O)— or —C(S)—;
  R<sup>2</sup> is selected from the group consisting of C<sub>1</sub>-C<sub>12</sub>alkenyl,
      C2-C12hydroxyalkyl,
                                                C2-C12hydroxyalkenyl,
      C<sub>2</sub>-C<sub>12</sub>alkoxyalkyl,
                                                        C<sub>3</sub>-C<sub>12</sub>cycloalkyl, 30
      C4-C12cycloalkylalkyl,
                                                            C7-C19aralkyl,
                                             aryl,
                                              C<sub>3</sub>-C<sub>12</sub>heterocyclylalkyl,
      C<sub>3</sub>-C<sub>12</sub>heterocyclyl,
      C_1-C_{12}heteroaryl, and C_3-C_{12}heteroarylalkyl;
  R<sup>3</sup> is selected from the group consisting of C<sub>1</sub>-C<sub>12</sub>alkyl,
                                                   C<sub>2</sub>-C<sub>12</sub>hydroxyalkyl, 35
C<sub>2</sub>-C<sub>12</sub>alkoxyalkyl,
      C2-C12alkenyl,
      C<sub>2</sub>-C<sub>12</sub>hydroxyalkenyl,
      C<sub>3</sub>-C<sub>12</sub>cycloalkyl,
                                    C<sub>4</sub>-C<sub>12</sub>cycloalkylalkyl,
                                                                         aryl,
      C7-C19aralkyl,
                                                     C<sub>3</sub>-C<sub>12</sub>heterocyclyl,
      C<sub>3</sub>-C<sub>12</sub>heterocyclylalkyl,
                                             C<sub>1</sub>-C<sub>12</sub>heteroaryl
                                                                           and
      C_3-C_{12}heteroarylalkyl, provided that when V is 40 —C(O)—, R^3 is not C_1-C_{12}alkyl;
   R4 and R5 are each hydrogen; and
  R<sup>6</sup>, R<sup>6a</sup>, R<sup>7</sup>, R<sup>7a</sup>, R<sup>8</sup>, R<sup>8a</sup>, R<sup>9</sup> and R<sup>9a</sup> are each hydrogen.
   4. The compound of claim 3 wherein:
   V is ---C(O)---;
                                                                                  45
  R^2 is C_7-C_{12}aralkyl optionally substituted by one or more
      substituents selected from halo, cyano, nitro, hydroxy,
      C_1-C_6alkyl, C_1-C_6trihaloalkyl and C_1-C_6trihaloalkoxy;
  R3 is phenyl optionally substituted by one or more substitu-
      ents selected from the group consisting of halo, cyano, 50
                hydroxy, C<sub>1</sub>-C<sub>6</sub>alkyl, C<sub>1</sub>-C<sub>6</sub>trihaloalkyl,
     C_1-C_6trihaloalkoxy, C_1-C_6alkylsulfonyl, -N(R^{12})_2, -OC(O)R^{12}, -C(O)OR^{12}, -S(O)_2N(R^{12})_2,
      cycloalkyl, heterocyclyl, heteroaryl and heteroarylcy-
      cloalkyl; and
  each R12 is independently selected from hydrogen,
      C_1-C_6alkyl, C_3-C_6cycloalkyl, aryl or aralkyl.
   5. The compound of claim 4 wherein:
  R<sup>2</sup> is C<sub>7</sub>-C<sub>12</sub>aralkyl optionally substituted by one or more
      substituents selected from halo, C1-C6alkyl, 60
      C1-C6trihaloalkyl and C1-C6trihaloalkoxy; and
  R<sup>3</sup> is phenyl optionally substituted by one or more substitu-
      ents selected from the group consisting of halo,
      C_1-C_6trihaloalkyl and C_1-C_6trihaloalkoxy.
  6. The compound of claim 5, namely, [4-(6-Phenethyloxy- 65
pyridazin-3-yl)-piperazin-1-yl]-(2-trifluoromethyl-phenyl)-
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methanone.

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7. The compound of claim 3 wherein:
   V \text{ is } \longrightarrow C(O) \longrightarrow;
   R^2 is C_1-C_{12}alkyl or C_2-C_{12}alkenyl;
   R<sup>3</sup> is phenyl optionally substituted by one or more substitu-
       ents selected from the group consisting of halo, cyano,
      nitro, hydroxy, C_1-C_6alkyl, C_1-C_6trihaloalkyl, C_1-C_6trihaloalkoxy, C_1-C_6alkylsulfonyl, -N(R^{12})_2, -OC(O)R^{12}, -C(O)OR^{12}, -S(O)_2N(R^{12})_2,
      cycloalkyl, heterocyclyl, heteroaryl and heteroarylcy-
      cloalkyl; and
   each R12 is independently selected from hydrogen,
       C_1-C_6alkyl, C_3-C_6cycloalkyl, aryl or aralkyl.
   8. The compound of claim 3 wherein:
   V \text{ is } \longrightarrow C(O) \longrightarrow
   R^2 is C_3-C_{12}cycloalkyl or C_4-C_{12}cycloalkylalkyl;
   R<sup>3</sup> is phenyl optionally substituted by one or more substitu-
      ents selected from the group consisting of halo, cyano,
      nitro, hydroxy, C_1-C_6alkyl, C_1-C_6trihaloalkyl, C_1-C_6trihaloalkoxy, C_1-C_6alkylsulfonyl, -N(R^{12})_2,
                                                        -S(O)_2N(R^{12})_2
                              -C(O)OR^{12}
        -OC(O)R^{12}
      cycloalkyl, heterocyclyl, heteroaryl and heteroarylcy-
   cloalkyl; and each R<sup>12</sup> is independently selected from hydrogen,
       C<sub>1</sub>-C<sub>6</sub>alkyl, C<sub>3</sub>-C<sub>6</sub>cycloalkyl, aryl or aralkyl.
   9. The compound of claim 8 wherein:
   R<sup>2</sup> is C<sub>4</sub>-C<sub>12</sub>cycloalkylalkyl; and
   R<sup>3</sup> is phenyl optionally substituted by one or more substitu-
       ents selected from the group consisting of halo,
       C_1-C_6trihaloalkyl and C_1-C_6trihaloalkoxy.
   10. The compound of claim 9, namely, {4-[6-(2-Cyclopro-
pyl-ethoxy)-pyridazin-3-yl]-piperazin-1-yl}-(2-trifluorom-
ethyl-phenyl)-methanone.
   11. The compound of claim 2 wherein:
   x and y are each 1;
   W is —S(O), — (where t is 0, 1 or 2);
V is —C(O)— or —C(S)—;
   R<sup>2</sup> is selected from the group consisting of C<sub>1</sub>-C<sub>12</sub>alkyl,
       C2-C12alkenyl,
                                                   C2-C12hydroxyalkyl,
       C2-C12hydroxyalkenyl,
                                                      C2-C12alkoxyalkyl,
                                     C<sub>4</sub>-C<sub>12</sub>cycloalkylalkyl,
      C<sub>3</sub>-C<sub>12</sub>cycloalkyl,
                                                                         aryl,
       C7-C12aralkyl,
                                                     C<sub>3</sub>-C<sub>12</sub>heterocyclyl,
       C<sub>3</sub>-C<sub>12</sub>heterocyclylalkyl,
                                             C<sub>1</sub>-C<sub>12</sub>heteroaryl,
       C<sub>3</sub>-C<sub>12</sub>heteroarylalkyl;
   R<sup>3</sup> is selected from the group consisting of C<sub>1</sub>-C<sub>12</sub>alkyl,
       C2-C12alkenyl,
                                                    C2-C12hydroxyalkyl,
       C2-C12hydroxyalkenyl,
                                                      C2-C12alkoxyalkyl,
       C<sub>3</sub>-C<sub>12</sub>cycloalkyl,
                                     C<sub>4</sub>-C<sub>12</sub>cycloalkylalkyl,
                                                                         aryl,
      C7-C12aralkyl,
                                                     C<sub>3</sub>-C<sub>12</sub>heterocyclyl,
      C<sub>3</sub>-C<sub>12</sub>heterocyclylalkyl,
                                             C<sub>1</sub>-C<sub>12</sub>heteroaryl
                                                                         and
      C_3-C_{12}heteroarylalkyl, provided that when V is —C(O)—, R^3 is not C_1-C_{12}alkyl;
   R4 and R5 are each hydrogen; and
   R^6, R^{6a}, R^7, R^{7a}, R^8, R^{8a}, R^9 and R^{9a} are each hydrogen.
   12. The compound of claim 11 wherein:
   V is ---C(O)--
   R<sup>2</sup> is C<sub>7</sub>-C<sub>12</sub>aralkyl optionally substituted by one or more
      substituents selected from halo, cyano, nitro, hydroxy,
       C1-C6alkyl, C1-C6trihaloalkyl and C1-C6trihaloalkoxy;
   R3 is phenyl optionally substituted by one or more substitu-
      ents selected from the group consisting of halo, cyano,
      nitro, hydroxy, C_1-C_6alkyl, C_1-C_6trihaloalkyl, C_1-C_6trihaloalkoxy, C_1-C_6alkylsulfonyl, -N(R^{12})_2, -OC(O)R^{12}, -C(O)OR^{12}, -S(O)_2N(R^{12})_2,
                                                        -S(O)_2N(R^{12})_2
      cycloalkyl, heterocyclyl, heteroaryl and heteroarylcy-
      cloalkyl; and
   each Ri2 is independently selected from hydrogen,
      C<sub>1</sub>-C<sub>6</sub>alkyl, C<sub>3</sub>-C<sub>6</sub>cycloalkyl, aryl or aralkyl.
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43 13. The compound of claim 12 wherein: R<sup>2</sup> is C<sub>7</sub>-C<sub>12</sub>aralkyl optionally substituted by one or more substituents selected from halo,  $C_1$ - $C_6$ alkyl,  $C_1$ - $C_6$ trihaloalkyl and  $C_1$ - $C_6$ trihaloalkoxy; and substituents R<sup>3</sup> is phenyl optionally substituted by one or more substitu- 5 ents selected from the group consisting of halo,  $C_1$ - $C_6$ trihaloalkyl and  $C_1$ - $C_6$ trihaloalkoxy. 14. The compound of claim 13 selected from the group consisting of the following: [4-(6-Phenethylsulfanyl-pyridazin-3-yl)-piperazin-1-yl]-(2-trifluoromethyl-phenyl)-methanone; {4-[6-(2-Phenyl-ethanesulfinyl)-pyridazin-3-yl]-piperazin-1-yl}-(2-trifluoromethyl-phenyl)-methanone; and {4-[6-(2-Phenyl-ethanesulfonyl)-pyridazin-3-yl]-piperazin-1-yl}-(2-trifluoromethyl-phenyl)-methanone. 15. The compound of claim 11 wherein: V is —C(O)—;  $R^2$  is  $C_1$ - $C_{12}$ alkyl or  $C_7$ - $C_{12}$ alkenyl; R<sup>3</sup> is phenyl optionally substituted by one or more substituents selected from the group consisting of halo, cyano, 20 hydroxy, C<sub>1</sub>-C<sub>6</sub>alkyl, C<sub>1</sub>-C<sub>6</sub>trihaloalkyl,  $C_1$ - $C_6$ trihaloalkoxy,  $C_1$ - $C_6$ alkylsulfonyl,  $-N(R^{12})_2$ ,  $-OC(O)R^{12}$ ,  $-C(O)OR^{12}$ ,  $-S(O)_2N(R^{12})_2$ , cycloalkyl, heterocyclyl, heteroaryl and heteroarylcycloalkyl; and each R12 is independently selected from hydrogen, C<sub>1</sub>-C<sub>6</sub>alkyl, C<sub>3</sub>-C<sub>6</sub>cycloalkyl, aryl or aralkyl. 16. The compound of claim 15 wherein R<sup>3</sup> is phenyl optionally substituted by one or more substituents selected from the group consisting of halo, C1-C6trihaloalkyl and 30 C1-C6trihaloalkoxy. 17. The compound of claim 16, namely, {4-[6-(3-Methyl $butylsulfanyl)-pyridazin-3-yl]-piperazin-1-yl\}-(2-trifluo-1-yl)-(2-trifl$ romethyl-phenyl)-methanone. 18. The compound of claim 2 wherein: x and y are each 1; W is  $--N(R^1)$ —; V is -C(O)—or -C(S)—; R<sup>1</sup> is hydrogen or C<sub>1</sub>-C<sub>6</sub>alkyl; R<sup>2</sup> is selected from the group consisting of C<sub>1</sub>-C<sub>12</sub>alkyl, C2-C12hydroxyalkyl, C2-C12alkenyl, C2-C12hydroxyalkenyl C2-C12alkoxyalkyl, C<sub>3</sub>-C<sub>12</sub>cycloalkyl, C<sub>4</sub>-C<sub>12</sub>cycloalkylalkyl, aryl, C7-C12aralkyl,  $C_3$ - $C_{12}$ heterocyclyl, 45 C<sub>3</sub>-C<sub>12</sub>heterocyclylalkyl, C<sub>1</sub>-C<sub>12</sub>heteroaryl, and C<sub>3</sub>-C<sub>12</sub>heteroarylalkyl; R<sup>3</sup> is selected from the group consisting of C<sub>1</sub>-C<sub>12</sub>alkyl, C2-C12alkenyl, C2-C12hydroxyalkyl. C2-C12hydroxyalkenyl, C<sub>2</sub>-C<sub>12</sub>alkoxyalkyl, 50 C<sub>4</sub>-C<sub>12</sub>cycloalkylalkyl, C<sub>3</sub>-C<sub>12</sub>cycloalkyl, aryl, C<sub>7</sub>-C<sub>12</sub>aralkyl, C<sub>3</sub>-C<sub>12</sub>heterocyclyl, C<sub>3</sub>-C<sub>12</sub>heterocyclylalkyl, C<sub>1</sub>-C<sub>12</sub>heteroaryl and  $C_3$ - $C_{12}$ heteroarylalkyl, provided that when V is -C(O)-,  $R^3$  is not  $C_1$ - $C_{12}$ alkyl; R4 and R5 are each hydrogen; and R<sup>6</sup>, R<sup>6a</sup>, R<sup>7</sup>, R<sup>7a</sup>, R<sup>8</sup>, R<sup>8a</sup>, R<sup>9</sup> and R<sup>9a</sup> are each hydrogen. 19. The compound of claim 18 wherein: V is ---C(O)--;R<sup>1</sup> is hydrogen or C<sub>1</sub>-C<sub>6</sub>alkyl; R<sup>2</sup> is C<sub>7</sub>-C<sub>12</sub> aralkyl optionally substituted by one or more substituents selected from halo, cyano, nitro, hydroxy, C1-C6alkyl, C1-C6trihaloalkyl and C1-C6trihaloalkoxy; R3 is phenyl optionally substituted by one or more substitu-

ents selected from the group consisting of halo, cyano, 65

 $C_1$ - $C_6$ trihaloalkoxy,  $C_1$ - $C_6$ alkylsulfonyl, — $N(R^{12})_2$ ,

hydroxy, C<sub>1</sub>-C<sub>6</sub>alkyl, C<sub>1</sub>-C<sub>6</sub>trihaloalkyl,

44 -C(O)OR12,  $--S(O)_2N(R^{12})_2$ ,  $--OC(O)R^{12}$ cycloalkyl, heterocyclyl, heteroaryl and heteroarylcycloalkyl; and each R12 is independently selected from hydrogen, C1-C6alkyl, C3-C6cycloalkyl, aryl or aralkyl. 20. The compound of claim 19 wherein R<sup>3</sup> is phenyl optionally substituted by one or more substituents selected from the group consisting of halo, C1-C6trihaloalkyl and C1-C6trihaloalkoxy. 21. The compound of claim 20 selected from the group consisting of the following: [4-(6-Phenethylamino-pyridazin-3-yl)-piperazin-1-yl]-(2-trifluoromethyl-phenyl)-methanone; and {-[6-(Methyl-phenethyl-amino)pyridazin-3-yl]-piperazin-1-yl}-(2-trifluoromethyl-phenyl)-methanone. 22. The compound of claim 18 wherein: V is ---C(O)---; R1 is hydrogen or C1-C6alkyl; R<sup>2</sup> is C<sub>1</sub>-C<sub>12</sub>alkyl, C<sub>2</sub>-C<sub>12</sub>alkenyl, C<sub>3</sub>-C<sub>12</sub>cycloalkyl or C<sub>4</sub>-C<sub>12</sub>cycloalkylalkyl; R3 is phenyl optionally substituted by one or more substituents selected from the group consisting of halo, cyano, cycloalkyl, heterocyclyl, heteroaryl and heteroarylcycloalkyl; and each R12 is independently selected from hydrogen, C<sub>1</sub>-C<sub>6</sub>alkyl, C<sub>3</sub>-C<sub>6</sub>cycloalkyl, aryl or aralkyl. 23. The compound of claim 2 wherein: x and y are each 1; W is  $-N(R^1)S(O)_2$ -; V is -C(O)— or -C(S)—;  $R^1$  is hydrogen or  $C_1$ - $C_6$ alkyl; R<sup>2</sup> is selected from the group consisting of C<sub>1</sub>-C<sub>12</sub>alkyl, C2-C12alkenyl, C2-C12hydroxyalkyl, C<sub>2</sub>-C<sub>12</sub>hydroxyalkenyl C2-C12alkoxyalkyl, C<sub>3</sub>-C<sub>12</sub>cycloalkyl, C<sub>4</sub>-C<sub>12</sub>cycloalkylalkyl, aryl, C<sub>7</sub>-C<sub>12</sub>aralkyl, C<sub>3</sub>-C<sub>12</sub>heterocyclyl, C<sub>3</sub>-C<sub>12</sub>heterocyclylalkyl,  $C_1$ - $C_{12}$ heteroaryl, C<sub>3</sub>-C<sub>12</sub>heteroarylalkyl; R<sup>3</sup> is selected from the group consisting of C<sub>1</sub>-C<sub>12</sub>alkyl, C<sub>2</sub>-C<sub>12</sub>alkenyl, C2-C12hydroxyalkyl, C2-C12alkoxyalkyl, C2-C12hydroxyalkenyl, C<sub>3</sub>-C<sub>12</sub>cycloalkyl, C<sub>4</sub>-C<sub>12</sub>cycloalkylalkyl, C<sub>7</sub>-C<sub>12</sub>aralkyl, C<sub>3</sub>-C<sub>12</sub>heterocyclyl, C<sub>3</sub>-C<sub>12</sub>heterocyclylalkyl, C<sub>1</sub>-C<sub>12</sub>heteroaryl and C<sub>3</sub>-C<sub>12</sub>heteroarylalkyl, provided that when V is -C(O)--, R3 is not C1-C12 alkyl; R4 and R5 are each hydrogen; and R<sup>6</sup>, R<sup>6a</sup>, R<sup>7</sup>, R<sup>7a</sup>, R<sup>8</sup>, R<sup>8a</sup>, R<sup>9</sup> and R<sup>9a</sup> are each hydrogen. 24. The compound of claim 23 wherein: V is —C(O)—; R<sup>1</sup> is hydrogen or C<sub>1</sub>-C<sub>6</sub>alkyl; R<sup>2</sup> is C<sub>1</sub>-C<sub>12</sub>alkyl, C<sub>2</sub>-C<sub>12</sub>alkenyl, C<sub>3</sub>-C<sub>12</sub>cycloalkyl or C<sub>4</sub>-C<sub>12</sub>cycloalkylalkyl; R<sup>3</sup> is phenyl optionally substituted by one or more substituents selected from the group consisting of halo, cyano, nitro, hydroxy, C<sub>1</sub>-C<sub>6</sub>alkyl, C<sub>1</sub>-C<sub>6</sub>trihaloalkyl,  $C_1$ - $C_6$ trihaloalkoxy,  $C_1$ - $C_6$ alkylsulfonyl,  $-N(R^{12})_2$ ,  $-OC(O)R^{12}$ ,  $-C(O)OR^{12}$ ,  $-S(O)_2N(R^{12})_2$ ,  $-S(O)_2N(R^{12})_2$ 

cycloalkyl, heterocyclyl, heteroaryl and heteroarylcy-

each R12 is independently selected from hydrogen,

C<sub>1</sub>-C<sub>6</sub>alkyl, C<sub>3</sub>-C<sub>6</sub>cycloalkyl, aryl or aralkyl.

cloalkyl; and

25. The compound of claim 24 wherein:

 $R^2$  is  $C_1$ - $C_{12}$ alkyl; and

R<sup>3</sup> is phenyl optionally substituted by one or more substituents selected from the group consisting of halo,  $C_1$ - $C_6$ trihaloalkyl and  $C_1$ - $C_6$ trihaloalkoxy.

26. The compound of claim 25, namely, Propane-1-sulfonic acid {6-[4-(2-trifluoromethyl-benzoyl)-piperazin-1yl]-pyridazin-3-yl}-amide.

27. The compound of claim 23 wherein:

V is —C(O)—;

R<sup>1</sup> is hydrogen or C<sub>1</sub>-C<sub>6</sub>alkyl;

R<sup>2</sup> is C<sub>7</sub>-C<sub>12</sub> aralkyl optionally substituted by one or more substituents selected from halo, cyano, nitro, hydroxyl,  $C_1$ - $C_6$ alkyl,  $C_1$ - $C_6$ trihaloalkyl and  $C_1$ - $C_6$ trihaloalkoxy;

R<sup>3</sup> is phenyl optionally substituted by one or more substitu- 15 rase with a compound of claim 2. ents selected from the group consisting of halo, cyano, nitro, hydroxyl, C<sub>1</sub>-C<sub>6</sub>alkyl, C<sub>1</sub>-C<sub>6</sub>trihaloalkyl and

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 $\begin{array}{lll} C_1\text{-}C_6\text{trihaloalkoxy}, & C_1\text{-}C_6\text{alkylsulfonyl}, & --N(R^{12})_2, \\ --OC(O)R^{12}, & --C(O)OR^{12}, & --S(O)_2N(R^{12})_2, \end{array}$ cycloalkyl, heterocyclyl, heteroaryl and heteroarylcycloalkyl; and each R<sup>12</sup> is independently selected from hydrogen,

C<sub>1</sub>-C<sub>6</sub>alkyl, C<sub>3</sub>-C<sub>6</sub>cycloalkyl, aryl or aralkyl.

28. A pharmaceutical composition comprising a pharmaceutically acceptable excipient and a therapeutically effective amoun of a compound of claim 2.

29. An in vivo method for inhibiting stearoyl-CoA desaturase, compising contacting a source of stearoyl-CoA desaturase with a compound of claim 1.

30. An in vivo method for inhibiting stearoyl-CoA desaturase, comprising contacting a source of stearoyl-CoA desatu-





#### **AMENDMENTS TO THE CLAIMS**

Please amend the claims as follows.

1. (Currently Amended) A compound of formula (I):

wherein:

x and y are each independently 1;

W is -O-, -C(O)O-, -N(R<sup>1</sup>)-, -S(O)<sub>t</sub>- (where t is 0, 1 or 2), -N(R<sup>1</sup>)S(O)<sub>2</sub>-, -OC(O)- or -C(O)-;

V is -C(O)-, -C(S)-, -C(O)N(R<sup>1</sup>)-, -C(O)O-, -S(O)<sub>2</sub>-, <u>or</u> -S(O)<sub>2</sub>N(R<sup>1</sup>)- <u>or -C(R<sup>11</sup>)H-</u>; each R<sup>1</sup> is independently selected from the group consisting of hydrogen,

C<sub>1</sub>-C<sub>12</sub>alkyl, C<sub>2</sub>-C<sub>12</sub>hydroxyalkyl, C<sub>4</sub>-C<sub>12</sub>cycloalkylalkyl and C<sub>7</sub>-C<sub>19</sub>aralkyl;

R<sup>2</sup> is selected from the group consisting of C<sub>1</sub>-C<sub>12</sub>alkyl, C<sub>2</sub>-C<sub>12</sub>alkenyl,

C<sub>2</sub>-C<sub>12</sub>hydroxyalkyl, C<sub>2</sub>-C<sub>12</sub>hydroxyalkenyl, C<sub>2</sub>-C<sub>12</sub>alkoxyalkyl, C<sub>3</sub>-C<sub>12</sub>cycloalkyl,

C<sub>4</sub>-C<sub>12</sub>cycloalkylalkyl, aryl, C<sub>7</sub>-C<sub>19</sub>aralkyl, C<sub>3</sub>-C<sub>12</sub>heterocyclyl, C<sub>3</sub>-C<sub>12</sub>heterocyclylalkyl,

C<sub>1</sub>-C<sub>12</sub>heteroaryl, and C<sub>3</sub>-C<sub>12</sub>heteroarylalkyl, provided that when W is -O-, R<sup>2</sup> is not C<sub>1</sub>-C<sub>12</sub>alkyl;

or R<sup>2</sup> is a multi-ring structure having 2 to 4 rings wherein the rings are independently selected from the group consisting of cycloalkyl, heterocyclyl, aryl and heteroaryl and where some or all of the rings may be fused to each other;

R³ is selected from the group consisting of  $C_1$ - $C_{12}$ alkyl,  $C_2$ - $C_{12}$ alkenyl,  $C_2$ - $C_{12}$ hydroxyalkyl,  $C_2$ - $C_{12}$ hydroxyalkenyl,  $C_2$ - $C_{12}$ alkoxyalkyl,  $C_3$ - $C_{12}$ cycloalkyl,  $C_4$ - $C_{12}$ cycloalkylalkyl, aryl,  $C_7$ - $C_{19}$ aralkyl,  $C_3$ - $C_{12}$ heterocyclyl,  $C_3$ - $C_{12}$ heterocyclylalkyl,  $C_1$ - $C_1$ -heteroaryl and  $C_3$ - $C_1$ -heteroarylalkyl, provided that when V is -C(O)- or -C(O)O-, R³ is not  $C_1$ - $C_1$ -alkyl;

or R<sup>3</sup> is a multi-ring structure having 2 to 4 rings wherein the rings are independently selected from the group consisting of cycloalkyl, heterocyclyl, aryl and heteroaryl and where some or all of the rings may be fused to each other;

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R<sup>4</sup> and R<sup>5</sup> are each independently selected from hydrogen, fluoro, chloro, methyl, methoxy, trifluoromethyl, cyano, nitro or -N(R<sup>13</sup>)<sub>2</sub>;

 $R^6$ ,  $R^6$ ,  $R^7$ ,  $R^{7a}$ ,  $R^8$ ,  $R^{8a}$ ,  $R^9$  and  $R^{9a}$  are each independently selected from hydrogen or  $C_1$ - $C_3$ alkyl;

R11-is-C1-C3alkyl; and

each R<sup>13</sup> is independently selected from hydrogen or C<sub>1</sub>-C<sub>6</sub>alkyl;

a stereoisomer, enantiomer or tautomer thereof, a pharmaceutically acceptable salt thereof, a pharmaceutical composition thereof or a prodrug thereof.

#### 2. - 9. (Canceled)

### 10. (Currently Amended) A compound of formula (Ia):

wherein:

x and y are each independently 1;

W is -O-, -C(O)O-, -N(R¹)-, -S(O)<sub>t</sub>- (where t is 0, 1 or 2), -N(R¹)S(O)<sub>2</sub>-, -OC(O)- or -C(O)-;

V is -C(O)-, -C(S)-, -C(O)N(R<sup>1</sup>)-, -C(O)O-, -S(O)<sub>2</sub>-,  $\underline{or}$  -S(O)<sub>2</sub>N(R<sup>1</sup>)-  $\underline{or}$  -C(R<sup>11</sup>)H-; each R<sup>1</sup> is independently selected from the group consisting of hydrogen,

 $C_1\text{-}C_{12}\text{alkyl},\ C_2\text{-}C_{12}\text{hydroxyalkyl},\ C_4\text{-}C_{12}\text{cycloalkylalkyl}\ \text{and}\ C_7\text{-}C_{19}\text{aralkyl};$ 

 $R^2$  is selected from the group consisting of  $C_1$ - $C_{12}$ alkyl,  $C_2$ - $C_{12}$ alkenyl,  $C_2$ - $C_{12}$ hydroxyalkyl,  $C_2$ - $C_{12}$ hydroxyalkenyl,  $C_2$ - $C_{12}$ alkoxyalkyl,  $C_3$ - $C_{12}$ cycloalkyl,  $C_3$ - $C_{12}$ heterocyclyl,  $C_3$ - $C_{12}$ heterocyclylalkyl,  $C_4$ - $C_{12}$ cycloalkylalkyl, aryl,  $C_7$ - $C_{19}$ aralkyl,  $C_3$ - $C_{12}$ heterocyclyl,  $C_3$ - $C_{12}$ heterocyclylalkyl,  $C_1$ - $C_1$ -heteroaryl, and  $C_3$ - $C_1$ -heteroarylalkyl, provided that, when W is -C(O)-,  $R^2$  can not be  $C_1$ - $C_6$ alkyl substituted by - $S(O)_t$ R<sup>14</sup> where  $R^{14}$  is hydrogen,  $C_1$ - $C_6$ alkyl,  $C_7$ - $C_{12}$ aralkyl, pyrazinyl, pyridinonyl, pyrrolidionyl or imidazolyl, provided that when W is -O-,  $R^2$  is not  $C_1$ - $C_{12}$ alkyl; or  $R^2$  is a multi-ring structure having 2 to 4 rings wherein the rings are

independently selected from the group consisting of cycloalkyl, heterocyclyl, aryl and heteroaryl and where some or all of the rings may be fused to each other;

R³ is selected from the group consisting of  $C_1$ - $C_{12}$ alkyl,  $C_2$ - $C_{12}$ alkenyl,  $C_2$ - $C_{12}$ hydroxyalkyl,  $C_2$ - $C_{12}$ hydroxyalkenyl,  $C_2$ - $C_{12}$ alkoxyalkyl,  $C_3$ - $C_{12}$ cycloalkyl,  $C_3$ - $C_{12}$ cycloalkylalkyl, aryl,  $C_7$ - $C_{19}$ aralkyl,  $C_3$ - $C_{12}$ heterocyclyl,  $C_3$ - $C_{12}$ heterocyclylalkyl,  $C_1$ - $C_1$ 2heteroaryl and  $C_3$ - $C_1$ 2heteroarylalkyl, provided that when V is -C(O)- or -C(O)O-, R³ is not  $C_1$ - $C_1$ 2alkyl;

or R<sup>3</sup> is a multi-ring structure having 2 to 4 rings wherein the rings are independently selected from the group consisting of cycloalkyl, heterocyclyl, aryl and heteroaryl and where some or all of the rings may be fused to each other;

 $R^4$  and  $R^5$  are each independently selected from hydrogen, fluoro, chloro, methyl, methoxy, trifluoromethyl, cyano, nitro or  $-N(R^{13})_2$ ;

 $R^6$ ,  $R^7$ ,  $R^7$ ,  $R^8$ ,  $R^8$ ,  $R^8$  and  $R^9$  are each independently selected from hydrogen or  $C_1$ - $C_3$ alkyl;

R<sup>11</sup>-is-C<sub>1</sub>-C<sub>3</sub>alkyl; and

each R<sup>13</sup> is independently selected from hydrogen or C<sub>1</sub>-C<sub>6</sub>alkyl;

a stereoisomer, enantiomer or tautomer thereof, a pharmaceutically acceptable salt thereof, a pharmaceutical composition thereof or a prodrug thereof.

11. (Previously Presented) The compound of Claim 10 wherein:

x and y are each 1;

W is -O-;

V is -C(O)- or -C(S)-;

 $R^2$  is selected from the group consisting of  $C_2$ - $C_{12}$ alkenyl,  $C_2$ - $C_{12}$ hydroxyalkyl,  $C_2$ - $C_{12}$ hydroxyalkenyl,  $C_2$ - $C_{12}$ alkoxyalkyl,  $C_3$ - $C_{12}$ cycloalkyl,  $C_4$ - $C_{12}$ cycloalkylalkyl, aryl,  $C_7$ - $C_{19}$ aralkyl,  $C_3$ - $C_{12}$ heterocyclyl,  $C_3$ - $C_{12}$ heterocyclylalkyl,  $C_1$ - $C_{12}$ heteroaryl, and  $C_3$ - $C_{12}$ heteroarylalkyl;

 $R^3$  is selected from the group consisting of  $C_1\text{-}C_{12}$ alkyl,  $C_2\text{-}C_{12}$ alkenyl,  $C_2\text{-}C_{12}$ hydroxyalkyl,  $C_2\text{-}C_{12}$ hydroxyalkenyl,  $C_2\text{-}C_{12}$ alkoxyalkyl,  $C_3\text{-}C_{12}$ cycloalkyl,  $C_4\text{-}C_{12}$ cycloalkylalkyl, aryl,  $C_7\text{-}C_{19}$ aralkyl,  $C_3\text{-}C_{12}$ heterocyclyl,  $C_3\text{-}C_{12}$ heterocyclylalkyl,  $C_1\text{-}C_{12}$ heteroaryl and  $C_3\text{-}C_{12}$ heteroarylalkyl, provided that when V is -C(O)-,  $R^3$  is not  $C_1\text{-}C_{12}$ alkyl;

R<sup>4</sup> and R<sup>5</sup> are each hydrogen; and

R<sup>6</sup>, R<sup>6a</sup>, R<sup>7</sup>, R<sup>7a</sup>, R<sup>8</sup>, R<sup>8a</sup>, R<sup>9</sup> and R<sup>9a</sup> are each hydrogen.

12. (original) The compound of Claim 11 wherein:

V is -C(O)-;

R<sup>2</sup> is C<sub>7</sub>-C<sub>12</sub>aralkyl optionally substituted by one or more substituents selected from halo, cyano, nitro, hydroxy, C<sub>1</sub>-C<sub>6</sub>alkyl, C<sub>1</sub>-C<sub>6</sub>trihaloalkyl and C<sub>1</sub>-C<sub>6</sub>trihaloalkoxy;

 $R^3$  is phenyl optionally substituted by one or more substituents selected from the group consisting of halo, cyano, nitro, hydroxy,  $C_1$ - $C_6$ alkyl,  $C_1$ - $C_6$ trihaloalkyl,  $C_1$ - $C_1$ -

each  $R^{12}$  is independently selected from hydrogen,  $C_1$ - $C_6$ alkyl,  $C_3$ - $C_6$ cycloalkyl, aryl or aralkyl.

13. (original) The compound of Claim 12 wherein:

 $R^2$  is  $C_7$ - $C_{12}$ aralkyl optionally substituted by one or more substituents selected from halo,  $C_1$ - $C_6$ alkyl,  $C_1$ - $C_6$ trihaloalkyl and  $C_1$ - $C_6$ trihaloalkoxy; and

 $R^3$  is phenyl optionally substituted by one or more substituents selected from the group consisting of halo,  $C_1$ - $C_6$ trihaloalkyl and  $C_1$ - $C_6$ trihaloalkoxy.

- 14. (original) The compound of Claim 13, namely, [4-(6-Phenethyloxy-pyridazin-3-yl)-piperazin-1-yl]-(2-trifluoromethyl-phenyl)-methanone.
  - 15. (original) The compound of Claim 11 wherein:

V is -C(O)-:

R<sup>2</sup> is C<sub>1</sub>-C<sub>12</sub>alkyl or C<sub>2</sub>-C<sub>12</sub>alkenyl;

 $R^3$  is phenyl optionally substituted by one or more substituents selected from the group consisting of halo, cyano, nitro, hydroxy,  $C_1$ - $C_6$ alkyl,  $C_1$ - $C_6$ trihaloalkyl,  $C_1$ - $C_6$ trihaloalkyl,  $C_1$ - $C_6$ trihaloalkyl,  $C_1$ - $C_6$ alkylsulfonyl, -N( $R^{12}$ )<sub>2</sub>, -OC(O) $R^{12}$ , -C(O)OR<sup>12</sup>, -S(O)<sub>2</sub>N( $R^{12}$ )<sub>2</sub>, cycloalkyl, heterocyclyl, heteroaryl and heteroarylcycloalkyl; and

each  $R^{12}$  is independently selected from hydrogen,  $C_1$ - $C_6$ alkyl,  $C_3$ - $C_6$ cycloalkyl, aryl or aralkyl.

16. (original) The compound of Claim 11 wherein:

V is -C(O)-;

R<sup>2</sup> is C<sub>3</sub>-C<sub>12</sub>cycloalkyl or C<sub>4</sub>-C<sub>12</sub>cycloalkylalkyl;

 $R^3$  is phenyl optionally substituted by one or more substituents selected from the group consisting of halo, cyano, nitro, hydroxy,  $C_1$ - $C_6$ alkyl,  $C_1$ - $C_6$ trihaloalkyl,  $C_1$ - $C_6$ trihaloalkyl,  $C_1$ - $C_6$ trihaloalkoxy,  $C_1$ - $C_6$ alkylsulfonyl, -N( $R^{12}$ )<sub>2</sub>, -OC(O) $R^{12}$ , -C(O)O $R^{12}$ , -S(O)<sub>2</sub>N( $R^{12}$ )<sub>2</sub>, cycloalkyl, heterocyclyl, heteroaryl and heteroarylcycloalkyl; and

each  $R^{12}$  is independently selected from hydrogen,  $C_1$ - $C_6$ alkyl,  $C_3$ - $C_6$ cycloalkyl, aryl or aralkyl.

17. (original) The compound of Claim 16 wherein:

R<sup>2</sup> is C<sub>4</sub>-C<sub>12</sub>cycloalkylalkyl; and

R<sup>3</sup> is phenyl optionally substituted by one or more substituents selected from the group consisting of halo, C₁-C₀trihaloalkyl and C₁-C₀trihaloalkoxy.

- 18. (original) The compound of Claim 17, namely, {4-[6-(2-Cyclopropyl-ethoxy)-pyridazin-3-yl]-piperazin-1-yl}-(2-trifluoromethyl-phenyl)-methanone.
  - 19. (Previously Presented) The compound of Claim 10 wherein:

x and y are each 1;

W is  $-S(O)_t$ - (where t is 0, 1 or 2);

V is -C(O)- or -C(S)-:

 $R^2$  is selected from the group consisting of  $C_1\text{-}C_{12}$  alkyl,  $C_2\text{-}C_{12}$  alkenyl,  $C_2\text{-}C_{12}$  hydroxyalkyl,  $C_2\text{-}C_{12}$  hydroxyalkenyl,  $C_2\text{-}C_{12}$  alkoxyalkyl,  $C_3\text{-}C_{12}$  cycloalkyl,  $C_4\text{-}C_{12}$  cycloalkyl, aryl,  $C_7\text{-}C_{12}$  aralkyl,  $C_3\text{-}C_{12}$  heterocyclyl,  $C_3\text{-}C_{12}$  heterocyclylalkyl,  $C_1\text{-}C_{12}$  heteroaryl, and  $C_3\text{-}C_{12}$  heteroarylalkyl;

 $R^3$  is selected from the group consisting of  $C_1\text{-}C_{12}$ alkyl,  $C_2\text{-}C_{12}$ alkenyl,  $C_2\text{-}C_{12}$ hydroxyalkyl,  $C_2\text{-}C_{12}$ hydroxyalkenyl,  $C_2\text{-}C_{12}$ alkoxyalkyl,  $C_3\text{-}C_{12}$ cycloalkyl,  $C_4\text{-}C_{12}$ cycloalkylalkyl, aryl,  $C_7\text{-}C_{12}$ aralkyl,  $C_3\text{-}C_{12}$ heterocyclyl,  $C_3\text{-}C_{12}$ heterocyclylalkyl,  $C_1\text{-}C_1$ heteroaryl and  $C_3\text{-}C_1$ heteroarylalkyl, provided that when V is -C(O)-,  $R^3$  is not  $C_1\text{-}C_1$ 2alkyl;

R<sup>4</sup> and R<sup>5</sup> are each hydrogen; and R<sup>6</sup>, R<sup>6a</sup>, R<sup>7</sup>, R<sup>7a</sup>, R<sup>8</sup>, R<sup>8a</sup>, R<sup>9</sup> and R<sup>9a</sup> are each hydrogen.

20. (original) The compound of Claim 19 wherein:

V is -C(O)-;

 $R^2$  is  $C_7$ - $C_{12}$ aralkyl optionally substituted by one or more substituents selected from halo, cyano, nitro, hydroxy,  $C_1$ - $C_6$ alkyl,  $C_1$ - $C_6$ trihaloalkyl and  $C_1$ - $C_6$ trihaloalkoxy;

 $R^3$  is phenyl optionally substituted by one or more substituents selected from the group consisting of halo, cyano, nitro, hydroxy,  $C_1$ - $C_6$ alkyl,  $C_1$ - $C_6$ trihaloalkyl,  $C_1$ - $C_6$ trihaloalkyl,  $C_1$ - $C_6$ trihaloalkyl,  $C_1$ - $C_6$ trihaloalkyl,  $C_1$ - $C_6$ alkylsulfonyl, -N( $R^{12}$ )<sub>2</sub>, -OC(O) $R^{12}$ , -C(O)OR<sup>12</sup>, -S(O)<sub>2</sub>N( $R^{12}$ )<sub>2</sub>, cycloalkyl, heterocyclyl, heteroaryl and heteroarylcycloalkyl; and

each  $R^{12}$  is independently selected from hydrogen,  $C_1$ - $C_6$ alkyl,  $C_3$ - $C_6$ cycloalkyl, aryl or aralkyl.

21. (original) The compound of Claim 20 wherein:

 $R^2$  is  $C_7$ - $C_{12}$ aralkyl optionally substituted by one or more substituents selected from halo,  $C_1$ - $C_6$ alkyl,  $C_1$ - $C_6$ trihaloalkyl and  $C_1$ - $C_6$ trihaloalkoxy; and

 $R^3$  is phenyl optionally substituted by one or more substituents selected from the group consisting of halo,  $C_1$ - $C_6$ trihaloalkyl and  $C_1$ - $C_6$ trihaloalkoxy.

22. (original) The compound of Claim 21 selected from the group consisting of the following:

[4-(6-Phenethylsulfanyl-pyridazin-3-yl)-piperazin-1-yl]-(2-trifluoromethyl-phenyl)-methanone;

{4-[6-(2-Phenyl-ethanesulfinyl)-pyridazin-3-yl]-piperazin-1-yl}-(2-trifluoromethyl-phenyl)-methanone; and

{4-[6-(2-Phenyl-ethanesulfonyl)-pyridazin-3-yl]-piperazin-1-yl}-(2-trifluoromethyl-phenyl)-methanone.

23. (original) The compound of Claim 19 wherein:

V is -C(O)-;

 $R^2$  is  $C_1$ - $C_{12}$ alkyl or  $C_2$ - $C_{12}$ alkenyl;

 $R^3$  is phenyl optionally substituted by one or more substituents selected from the group consisting of halo, cyano, nitro, hydroxy,  $C_1$ - $C_6$ alkyl,  $C_1$ - $C_6$ trihaloalkyl,  $C_1$ - $C_6$ trihaloalkoxy,  $C_1$ - $C_6$ alkylsulfonyl, -N( $R^{12}$ )<sub>2</sub>, -OC(O) $R^{12}$ , -C(O)OR<sup>12</sup>, -S(O)<sub>2</sub>N( $R^{12}$ )<sub>2</sub>, cycloalkyl, heterocyclyl, heteroaryl and heteroarylcycloalkyl; and

each R<sup>12</sup> is independently selected from hydrogen, C<sub>1</sub>-C<sub>6</sub>alkyl, C<sub>3</sub>-C<sub>6</sub>cycloalkyl,

aryl or aralkyl.

24. (original) The compound of Claim 23 wherein  $R^3$  is phenyl optionally substituted by one or more substituents selected from the group consisting of halo,  $C_1$ - $C_6$ trihaloalkyl and  $C_1$ - $C_6$ trihaloalkoxy.

- 25. (original) The compound of Claim 24, namely, {4-[6-(3-Methyl-butylsulfanyl)-pyridazin-3-yl]-piperazin-1-yl}-(2-trifluoromethyl-phenyl)-methanone.
  - 26. (Previously Presented) The compound of Claim 10 wherein:

x and y are each 1;

W is  $-N(R^1)$ -;

V is -C(O)- or -C(S)-;

R<sup>1</sup> is hydrogen or C<sub>1</sub>-C<sub>6</sub>alkyl;

 $R^2$  is selected from the group consisting of  $C_1\text{-}C_{12}$  alkyl,  $C_2\text{-}C_{12}$  alkenyl,  $C_2\text{-}C_{12}$  hydroxyalkyl,  $C_2\text{-}C_{12}$  hydroxyalkenyl,  $C_2\text{-}C_{12}$  alkoxyalkyl,  $C_3\text{-}C_{12}$  cycloalkyl,  $C_4\text{-}C_{12}$  cycloalkylalkyl, aryl,  $C_7\text{-}C_{12}$  aralkyl,  $C_3\text{-}C_{12}$  heterocyclyl,  $C_3\text{-}C_{12}$  heterocyclylalkyl,  $C_1\text{-}C_{12}$  heteroaryl, and  $C_3\text{-}C_{12}$  heteroarylalkyl;

 $R^3$  is selected from the group consisting of  $C_1\text{-}C_{12}$  alkyl,  $C_2\text{-}C_{12}$  alkenyl,  $C_2\text{-}C_{12}$  hydroxyalkyl,  $C_2\text{-}C_{12}$  hydroxyalkenyl,  $C_2\text{-}C_{12}$  alkoxyalkyl,  $C_3\text{-}C_{12}$  cycloalkyl,  $C_4\text{-}C_{12}$  cycloalkylalkyl, aryl,  $C_7\text{-}C_{12}$  aralkyl,  $C_3\text{-}C_{12}$  heterocyclyl,  $C_3\text{-}C_{12}$  heterocyclylalkyl,  $C_1\text{-}C_1$  heteroaryl and  $C_3\text{-}C_1$  heteroarylalkyl, provided that when V is -C(O)-,  $R^3$  is not  $C_1\text{-}C_1$  alkyl;

R<sup>4</sup> and R<sup>5</sup> are each hydrogen; and R<sup>6</sup>, R<sup>6a</sup>, R<sup>7</sup>, R<sup>7a</sup>, R<sup>8</sup>, R<sup>8a</sup>, R<sup>9</sup> and R<sup>9a</sup> are each hydrogen.

27. (original) The compound of Claim 26 wherein:

V is -C(O)-;

R¹ is hydrogen or C₁-C₀alkyl;

 $R^2$  is  $C_7$ - $C_{12}$ aralkyl optionally substituted by one or more substituents selected from halo, cyano, nitro, hydroxy,  $C_1$ - $C_6$ alkyl,  $C_1$ - $C_6$ trihaloalkyl and  $C_1$ - $C_6$ trihaloalkoxy;

R<sup>3</sup> is phenyl optionally substituted by one or more substituents selected from the group consisting of halo, cyano, nitro, hydroxy, C<sub>1</sub>-C<sub>6</sub>alkyl, C<sub>1</sub>-C<sub>6</sub>trihaloalkyl, C<sub>1</sub>-C<sub>6</sub>trihaloalkoxy,

 $C_1$ - $C_6$ alkylsulfonyl, -N(R<sup>12</sup>)<sub>2</sub>, -OC(O)R<sup>12</sup>, -C(O)OR<sup>12</sup>, -S(O)<sub>2</sub>N(R<sup>12</sup>)<sub>2</sub>, cycloalkyl, heterocyclyl, heteroaryl and heteroarylcycloalkyl; and

each  $R^{12}$  is independently selected from hydrogen,  $C_1$ - $C_6$ alkyl,  $C_3$ - $C_6$ cycloalkyl, aryl or aralkyl.

- 28. (original) The compound of Claim 27 wherein  $R^3$  is phenyl optionally substituted by one or more substituents selected from the group consisting of halo,  $C_1$ - $C_6$ trihaloalkyl and  $C_1$ - $C_6$ trihaloalkoxy.
- 29. (original) The compound of Claim 28 selected from the group consisting of the following:



[4-(6-Phenethylamino-pyridazin-3-yl)-piperazin-1-yl]-(2-trifluoromethyl-phenyl)-methanone; and [4-[6-(Methyl-phenethyl-amino)-pyridazin-3-yl]-piperazin-1-yl}-(2-trifluoromethyl-phenyl)-methanone.

30. (original) The compound of Claim 26 wherein:

V is -C(O)-;

R<sup>1</sup> is hydrogen or C<sub>1</sub>-C<sub>6</sub>alkyl;

R<sup>2</sup> is C<sub>1</sub>-C<sub>12</sub>alkyl, C<sub>2</sub>-C<sub>12</sub>alkenyl, C<sub>3</sub>-C<sub>12</sub>cycloalkyl or C<sub>4</sub>-C<sub>12</sub>cycloalkylalkyl;

 $R^3$  is phenyl optionally substituted by one or more substituents selected from the group consisting of halo, cyano, nitro, hydroxy,  $C_1$ - $C_6$ alkyl,  $C_1$ - $C_6$ trihaloalkyl,  $C_1$ - $C_6$ trihaloalkyl,  $C_1$ - $C_6$ trihaloalkyl,  $C_1$ - $C_6$ alkylsulfonyl, -N( $R^{12}$ )<sub>2</sub>, -OC(O) $R^{12}$ , -C(O)OR<sup>12</sup>, -S(O)<sub>2</sub>N( $R^{12}$ )<sub>2</sub>, cycloalkyl, heterocyclyl, heteroaryl and heteroarylcycloalkyl; and

each  $R^{12}$  is independently selected from hydrogen,  $C_1$ - $C_6$ alkyl,  $C_3$ - $C_6$ cycloalkyl, aryl or aralkyl.

31. (Previously Presented) The compound of Claim 10 wherein:

x and y are each 1;

W is  $-N(R^1)S(O)_2$ -;

V is -C(O)- or -C(S)-;

R<sup>1</sup> is hydrogen or C<sub>1</sub>-C<sub>6</sub>alkvl:

 $R^2$  is selected from the group consisting of  $C_1$ - $C_{12}$ alkyl,  $C_2$ - $C_{12}$ alkenyl,  $C_2$ - $C_{12}$ hydroxyalkyl,  $C_2$ - $C_{12}$ hydroxyalkyl,  $C_3$ - $C_{12}$ cycloalkyl,

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 $C_4$ - $C_{12}$ cycloalkylalkyl, aryl,  $C_7$ - $C_{12}$ aralkyl,  $C_3$ - $C_{12}$ heterocyclyl,  $C_3$ - $C_{12}$ heterocyclylalkyl,  $C_1$ - $C_{12}$ heteroaryl, and  $C_3$ - $C_{12}$ heteroarylalkyl;

 $R^3$  is selected from the group consisting of  $C_1\text{-}C_{12}$ alkyl,  $C_2\text{-}C_{12}$ alkenyl,  $C_2\text{-}C_{12}$ hydroxyalkyl,  $C_2\text{-}C_{12}$ hydroxyalkenyl,  $C_2\text{-}C_{12}$ alkoxyalkyl,  $C_3\text{-}C_{12}$ cycloalkyl,  $C_4\text{-}C_{12}$ cycloalkylalkyl, aryl,  $C_7\text{-}C_{12}$ aralkyl,  $C_3\text{-}C_{12}$ heterocyclyl,  $C_3\text{-}C_{12}$ heterocyclylalkyl,  $C_1\text{-}C_1$ heteroaryl and  $C_3\text{-}C_1$ heteroarylalkyl, provided that when V is -C(O)-,  $R^3$  is not  $C_1\text{-}C_1$ alkyl;

R<sup>4</sup> and R<sup>5</sup> are each hydrogen; and R<sup>6</sup>, R<sup>6a</sup>, R<sup>7</sup>, R<sup>7a</sup>, R<sup>8</sup>, R<sup>8a</sup>, R<sup>9</sup> and R<sup>9a</sup> are each hydrogen.

32. (original) The compound of Claim 31 wherein:

V is -C(O)-;

R<sup>1</sup> is hydrogen or C<sub>1</sub>-C<sub>6</sub>alkyl;

R<sup>2</sup> is C<sub>1</sub>-C<sub>12</sub>alkyl, C<sub>2</sub>-C<sub>12</sub>alkenyl, C<sub>3</sub>-C<sub>12</sub>cycloalkyl or C<sub>4</sub>-C<sub>12</sub>cycloalkylalkyl;

 $R^3$  is phenyl optionally substituted by one or more substituents selected from the group consisting of halo, cyano, nitro, hydroxy,  $C_1$ - $C_6$ alkyl,  $C_1$ - $C_6$ trihaloalkyl,  $C_1$ - $C_6$ trihaloalkoxy,  $C_1$ - $C_6$ alkylsulfonyl, -N( $R^{12}$ )<sub>2</sub>, -OC(O) $R^{12}$ , -C(O)OR<sup>12</sup>, -S(O)<sub>2</sub>N( $R^{12}$ )<sub>2</sub>, cycloalkyl, heterocyclyl, heteroaryl and heteroarylcycloalkyl; and

each  $R^{12}$  is independently selected from hydrogen,  $C_1$ - $C_6$ alkyl,  $C_3$ - $C_6$ cycloalkyl, aryl or aralkyl.

33. (original) The compound of Claim 32 wherein:

R<sup>2</sup> is C<sub>1</sub>-C<sub>1</sub>, alkyl; and

R<sup>3</sup> is phenyl optionally substituted by one or more substituents selected from the group consisting of halo, C<sub>1</sub>-C<sub>6</sub>trihaloalkyl and C<sub>1</sub>-C<sub>6</sub>trihaloalkoxy.

- 34. (original) The compound of Claim 33, namely, Propane-1-sulfonic acid {6-[4-(2-trifluoromethyl-benzoyl)-piperazin-1-yl]-pyridazin-3-yl}-amide.
  - 35. (original) The compound of Claim 31 wherein:

V is -C(O)-;

R<sup>1</sup> is hydrogen or C<sub>1</sub>-C<sub>6</sub>alkyl;

 $R^2$  is  $C_{\mathcal{T}}C_{12}$  aralkyl optionally substituted by one or more substituents selected



from halo, cyano, nitro, hydroxy, C<sub>1</sub>-C<sub>6</sub>alkyl, C<sub>1</sub>-C<sub>6</sub>trihaloalkyl and C<sub>1</sub>-C<sub>6</sub>trihaloalkoxy;

 $R^3$  is phenyl optionally substituted by one or more substituents selected from the group consisting of halo, cyano, nitro, <u>hydroxy</u>,  $C_1$ - $C_6$ alkyl, <u>C\_1</u>- $C_6$ trihaloalkyl, <u>C\_1</u>- $C_6$ trihaloalkoxy,  $C_1$ - $C_6$ alkylsulfonyl, -N( $R^{12}$ )<sub>2</sub>, -OC(O) $R^{12}$ , -C(O)OR<sup>12</sup>, -S(O)<sub>2</sub>N( $R^{12}$ )<sub>2</sub>, cycloalkyl, heterocyclyl, heteroaryl and heteroarylcycloalkyl; and

each  $R^{12}$  is independently selected from hydrogen,  $C_1$ - $C_6$ alkyl,  $C_3$ - $C_6$ cycloalkyl, aryl or aralkyl.

36. (Canceled).



- 37. (original) A pharmaceutical composition comprising a pharmaceutically acceptable excipient and a therapeutically effective amount of a compound of Claim 10.
- 38. (New) A method for inhibiting stearoyl-CoA desaturase, comprising contacting a source of stearoyl-CoA desaturase with a compound of claim 1.
- 39. (New) A method for inhibiting stearoyl-CoA desaturase, comprising contacting a source of stearoyl-CoA desaturase with a compound of claim 10.

#### UNITED STATES PATENT AND TRADEMARK OFFICE CERTIFICATE OF CORRECTION

Page 1 of 2

PATENT NO.

7,514,436

APPLICATION NO. :

10/566,856

ISSUE DATE

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INVENTOR(S)

Heinz W. Gschwend et al.

It is certified that an error appears or errors appear in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

In the Claims:

In Claim 1, column 40, line 22, " $R_{7a}$ " should be  $-R^{7a}$ -.

In Claim 15, column 43, line 17, " $C_7$ - $C_{12}$ " should be  $-C_2$ - $C_{12}$ -.

In Claim 21, column 44, line 14, "{-[6-(Methyl-phenethyl-amino)pyridazin-3-

yl]" should be -{4-[6-(Methyl-phenethyl-amino)-pyridazin-3-yl]-.

In Claim 27, column 45, line 13, the word "hydroxyl" should be **-hydroxy-**.

In Claim 27, column 45, line 17, the word "hydroxyl" should be **-hydroxy**-.

#### UNITED STATES PATENT AND TRADEMARK OFFICE CERTIFICATE OF CORRECTION

Page 2 of 2

PATENT NO.

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INVENTOR(S)

Heinz W. Gschwend et al.

It is certified that an error appears or errors appear in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

In Claim 27, column 45, line 17, "C<sub>1</sub>-C<sub>6</sub>trihaloalkyl and" should be --C<sub>1</sub>-

C6trihaloalkyl,--.

In Claim 28, column 46, line 9, the word "amoun" should be --amount--.

Attorney Docket No.: 17243/004001

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Application No. (if known): 10/566,856

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